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Patent No.
203/268

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of:

BOEHM, et al.

Serial No.: 08/141,496

Filed: October 22, 1993

For: COMPOUNDS HAVING SELECTIVE
ACTIVITY FOR RETINOID X RECEPTORS,
AND MEANS FOR MODULATION OF
PROCESSES MEDIATED BY RETINOID X
RECEPTORS

)
) Group Art Unit: 1621

)
) Examiner: Killos, P.

COMMUNICATION PURSUANT TO 37 C.F.R. § 1.607 REQUEST TO
DECLARE INTERFERENCE WITH U.S. PATENT NOS. 5,466,861 AND
5,837,725 AND NOTICE OF PROPOSED COUNTS

Honorable Commissioner for Patents and Trademarks
Washington, D.C. 20231

Sir:

Applicants hereby seek to have an interference declared between U.S. Application
Serial No. 08/141,496 ("the '496 Application"), filed October 22, 1993, and two U.S.
Patents, both to Dawson, et al: U.S. Patent No. 5,466,861 ("the '861 Patent") issued
November 14, 1995 (included herewith as Exhibit A) and U.S. Patent No. 5,837,725 ("the

CERTIFICATE OF FILING
(37 C.F.R. §1.6(c))

I hereby certify that this paper (along with any referred to as being attached or enclosed) is being hand delivered to
United States Patent and Trademark Office, Group 1621 at Crystal Mall 1, Arlington, Virginia.

August 10, 1999
Date of Deposit

Michael T. Wise

Name of Person Filing Paper

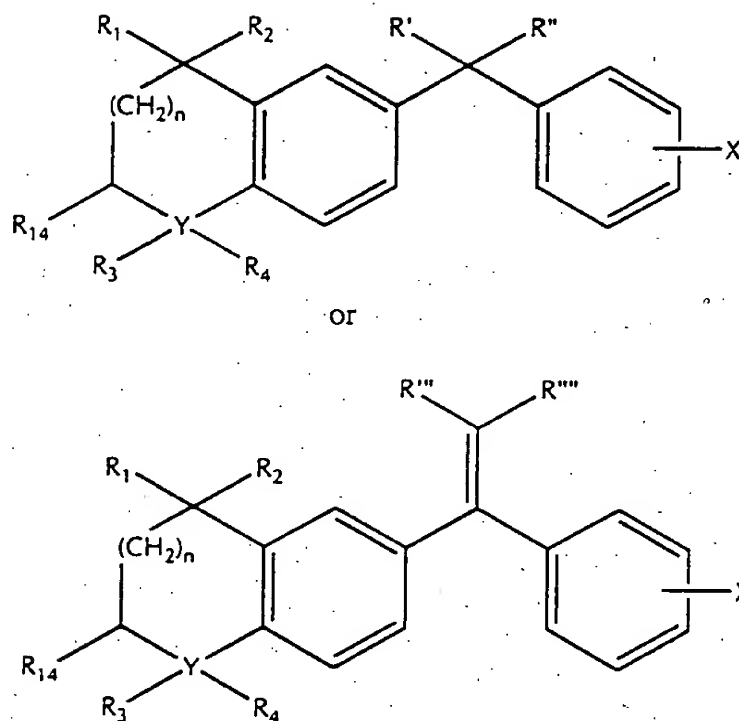
Michael T. Wise
Signature of Person Filing Paper

'725 Patent") issued November 17, 1998 (included herewith as Exhibit B).

Applicants present four patentably distinct proposed counts.

Proposed Count 1

A compound having the formula:



wherein

R₁ and R₂, each independently, represent hydrogen or lower alkyl having 1-4 carbon atoms;

Y represents C, O, S, or N;

R₃ represents hydrogen or lower alkyl having 1-4 carbon atoms where Y is C or N;

R₄ represents hydrogen or lower alkyl having 1-4 carbon atoms where Y is C, but R₄ does not exist if Y is N, and neither R₃ or R₄ exist if Y is S or O;

R₁₄ represents hydrogen or lower alkyl having 1-4 carbon atoms;

R' and R'', each independently, represent hydrogen or lower alkyl having 1-4 carbon atoms, but both are not hydrogen;

or R' or R'' taken together form a cyclopropyl or cycloalkyl group having 3-10 carbons, and wherein the cyclopropyl and cycloalkyl groups can be substituted with lower alkyl having 1-4 carbons;

R''' and R''', each independently, represent hydrogen or lower alkyl having 1-4 carbon atoms, but both are not hydrogen;

or R''' and R''' taken together form a cyclopropyl or cycloalkyl group having 3-10 carbons, and wherein the cyclopropyl and cycloalkyl groups can be substituted with lower alkyl having 1-4 carbons;

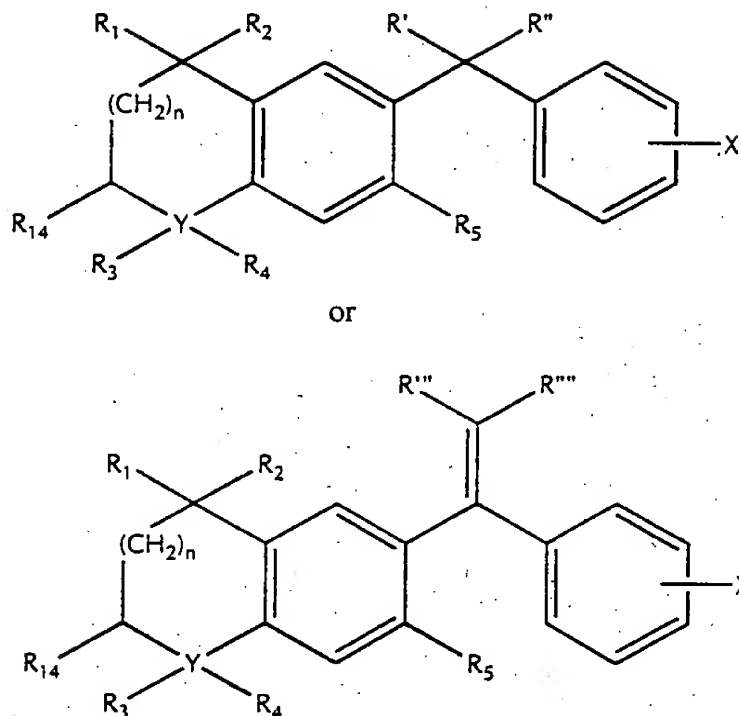
X is COOH and can originate from C 3, 4 or 5 on the ring;

n = 0-1;

and the pharmaceutically acceptable ester, amides and salts of the compound.

Proposed Count 2

A compound having the formula:



wherein

R_1 and R_2 , each independently, represent hydrogen or lower alkyl having 1-4 carbon atoms;

Y represents C, O, S, or N;

R_3 represents hydrogen or lower alkyl having 1-4 carbon atoms where Y is C or N;

R_4 represents hydrogen or lower alkyl having 1-4 carbon atoms where Y is C, but R_4 does not exist if Y is N, and neither R_3 or R_4 exist if Y is S or O;

R' , R'' , R''' and R'''' represent hydrogen, or R' and R'' taken together form an oxo

(keto) or methano;

R_5 represents a lower alkyl having 1-4 carbons or OR_7 ;

R_7 represents hydrogen or a lower alkyl having 1-6 carbons;

R_{14} represents hydrogen or lower alkyl having 1-4 carbon atoms;

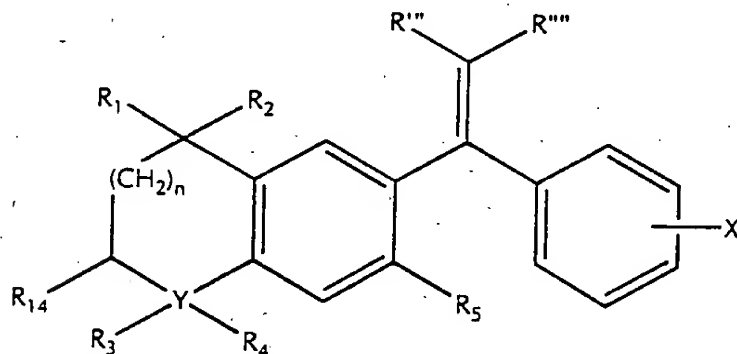
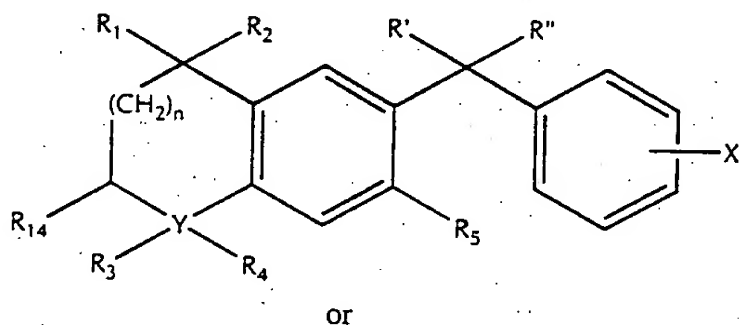
X is $COOH$ and can originate from C 3, 4 or 5 on the ring;

$n = 0-1$;

and the pharmaceutically acceptable ester, amides and salts of the compound.

Proposed Count 3

A compound having the formula:



wherein

R_1 and R_2 , each independently, represent hydrogen or lower alkyl having 1-4 carbon

atoms;

Y represents C, O, S, or N;

R₃ represents hydrogen or lower alkyl having 1-4 carbon atoms where Y is C or N;

R₄ represents hydrogen or lower alkyl having 1-4 carbon atoms where Y is C, but R₄ does not exist if Y is N, and neither R₃ or R₄ exist if Y is S or O;

R' and R'', each independently, represent hydrogen or lower alkyl having 1-4 carbon atoms, but at least one is not hydrogen;

or R' or R'' taken together form a cyclopropyl or cycloalkyl group having 3-10 carbons, and wherein the cyclopropyl and cycloalkyl groups can be substituted with lower alkyl having 1-4 carbons;

R''' and R''', each independently, represent hydrogen or lower alkyl having 1-4 carbon atoms, but at least one is not hydrogen;

or R''' and R''' taken together form a cyclopropyl or cycloalkyl group having 3-10 carbons, and wherein the cyclopropyl and cycloalkyl groups can be substituted with lower alkyl having 1-4 carbons;

R₅ represents a lower alkyl having 1-4 carbons or OR₇;

R₇ represents hydrogen or a lower alkyl having 1-6 carbons;

R₁₄ represents hydrogen or lower alkyl having 1-4 carbon atoms;

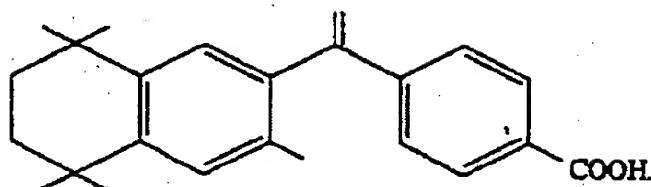
X is COOH and can originate from C 3, 4 or 5 on the ring;

n = 0-1;

and the pharmaceutically acceptable ester, amides and salts of the compound.

Proposed Count 4

A compound having the structural formula



and the pharmaceutically acceptable esters, amides and salts of the compound.

Claims Corresponding to the Counts

Concurrently herewith Applicants have filed a Preliminary Amendment to their above-identified pending '496 Application. The Preliminary Amendment cancels all previously pending claims and presents new claims 64-70.

Applicants submit that the '861 Patent claims corresponding to proposed count 1 include at least claims 1, 2, 3, 4, 5, 6, 7, 8, 10, 11, 14, 15, 16, 17, 18, 19, 20, 21, 22 and 23. The '725 Patent claims corresponding to proposed count 1 include at least claims 1, 2, 3, 4, 5, 7, 10, 11, 12, 13, 14, 15, 26, 27, 28 and 29. The '496 Application's claims corresponding to proposed count 1 are claims 64 and 67.

The '861 Patent claims corresponding to proposed count 2 include at least claims 1, 2, 3, 4, 6, 7, 12, 15 and 23. The '725 Patent claims corresponding to proposed count 2 include at least claims 1, 2, 3, 5, 7, 10, 11, 13, 14, 26, 27, 28 and 29. The '496 Application's claims corresponding to proposed count 2 are claims 65 and 68.

The '861 Patent claims corresponding to proposed count 3 include at least claims 1,

2, 3, 4, 5, 6, 7, 8, 15, and 23. The '725 Patent claims corresponding to proposed count 3 include at least claims 1, 2, 3, 5, 7, 10, 11, 12, 13, 14, 15, 26, 27, 28 and 29. The '496 Application's claims corresponding to proposed count 3 are claims 66 and 69.

Claim 13 in the '861 Patent corresponds to proposed count 4. Claims 70 in the '496 Application corresponds to proposed count 4. No claims in the '725 Patent correspond to proposed count 4.

Explanation of why each claim corresponds to proposed count.

Proposed count 1.

The genus of compounds defined by proposed count 1 includes compounds with the generic structural formula of proposed count 1, having a bulky substituent at the bridging carbon but no substituent at position R5 (that is R5 is H). Proposed count 1 excludes certain Markush groups present, *inter alia*, in claim 1 of the '861 Patent, and claim 1 of the '725 Patent, such that proposed count 1 defines a genus of compounds narrower than the class of compounds defined by those claims.¹ This is in part necessary to avoid the prior art.²

'861 Patent

Claim 1 of the '861 Patent defines a class of compounds which includes compounds within the scope of the genus defined by proposed count 1. Claim 1, therefore, corresponds to proposed count 1.

¹ Substantial overlap in the subject matter claimed in the '861 and '725 Patents required the filing of a terminal disclaimer in the '725 Patent.

² Several of the '861 patent's claims (including, for example, claim 1), and of the '725 patent's claims (including, for example, claim 1), read on Maignan, et al., GB2197316A included herewith as Exhibit C.

Claim 2 of the '861 Patent is directed to pharmaceutical compositions that include the compounds of claim 1, and therefore corresponds to proposed count 1.

Claim 3 of the '861 Patent depends from claim 1, and narrows the class of compounds to those having R1 ortho to R2, and R1 and R2 linked together to form a 5- or 6-membered cycloalkylene ring. The claim includes compounds within the scope of proposed count 1.

Claim 4 of the '861 Patent depends from claim 3 and further narrows the class of compounds having R1 ortho to R2, and R1 and R2 linked together to form a 6-membered cycloalkylene ring. The claim includes compounds within the scope of proposed count 1.

Claims 5, 6, 7, 8, 10, 11, 14, 16 depend from claim 4 and define further subclasses and species of compounds within the scope of proposed count 1.

Claim 15 defines a pharmaceutical composition including a compound within the scope of claim 4.

Claims 16 - 22 explicitly exclude compounds having a substituent at R5 (i.e. $n = o$). To the extent they define compounds having a bulky substituent at the bridging carbon while avoiding the prior art, they fall within the scope of proposed count 1.

Claim 16 explicitly excludes compounds having a substituent at position R5, substantiating the fact that such compounds, to which proposed count 1 is directed, represent a proper genus.

Claim 17 depends from claim 16, and defines a subclass that includes compounds within the scope of proposed count 1.

Claim 18 depends from claim 17, and further defines compounds which explicitly have bulky substituents at the bridging carbon. As claim 17 depends from claim 16, which defines compounds having no substituent at R5, the compounds defined by claim 18 have a bulky substituent at the bridging carbon and no substituent at R5, the defining characteristics of the compounds defined by proposed count 1.

Claims 19, 20 and 22 of the '861 Patent depend from claim 16, and define further subclasses that include compounds within the scope of proposed count 1.

Claim 21 depends from claim 20, and further defines compounds which explicitly have bulky substituents at the bridging carbon. As claim 20 depends from claim 16, which defines compounds having no substituent at R5. Therefore the compounds defined by claim 21 have a bulky substituent at the bridging carbon and no substituent at R5, the defining characteristics of the compounds defined by proposed count 1.

Claim 23 of the '861 Patent is directed to pharmaceutical compositions. The compositions of claim 23 include a compound within the class defined in claim 23. This class of compounds is broader than the class of compounds defined by claim 1. The pharmaceutical compositions defined by claim 23 include compounds within the scope of proposed count 1, therefore claim 23 corresponds to proposed count 1.

'725 Patent

Claim 1 of the '725 Patent corresponds to proposed count 1, since the class of compounds defined by claim 1 includes compounds within the genus defined by proposed count 1.

Claim 2 of the '725 Patent depends from claim 1 and narrows the class of compounds defined by claim 1 to compounds wherein R1 is ortho to R2, and R1 and R2 are linked together to form a 5- or 6-membered cycloalkylene ring. The claim includes compounds within the scope of proposed count 1.

Claim 3 of the '725 Patent depends from claim 2 and further narrows the class of compounds wherein R1 is ortho to R2 and R1, and R2 are linked together to form a 6-membered cycloalkylene ring. The claim includes compounds within the scope of proposed count 1.

Claims 4, 5, 10 and 13 depend from claim 3. Claim 4 explicitly excludes compounds having a substituent at position R5, substantiating the fact that such compounds, to which proposed count 1 is directed, represent a proper genus.

Claim 5 further narrows the class of compounds of claim 3 to those that have an R4 consisting of one of two aromatic carboxylic acids: a pyridine carboxylic acid or benzoic acid. The compounds defined by proposed count 1 have a benzoic acid at this position. Thus, claim 5 includes compounds within the scope of proposed count 1.

Claims 10 and 13 further narrow the class of compounds of claim 3 to specific R3 substituents. As the class of compounds defined by these claims include compounds having a "bulky" substituents at R3 and an H at R5 - the defining characteristic of the compounds of proposed count 1- these claims correspond to proposed count 1.

Claims 7, 11 and 14 depend from claim 5. Claim 7 narrows the class of compounds of claim 5 to those where R4 is benzoic acid. Compounds of proposed count

1 also have a benzoic acid at this position.

Claims 11 and 14 further narrow the class of compounds of claim 5 to specific R3 substituents. As the classes defined by these claims include compounds having a "bulky" substituents at R3, these claims also correspond to proposed count 1.

Claims 12 and 15 depend from claims 11 and 14, respectively, and further narrow the R3 substituent to a few species. As all these species of R3 are "bulky" these claims also correspond to proposed count 1.

Claims 26 and 27 are directed, *inter alia*, to pharmaceutical compositions including a compound within the class of compounds defined by claims 1 and 3, respectively. The pharmaceutical compositions defined by claims 26 and 27 include compounds within the genus of compounds defined by proposed count 1 and therefore correspond thereto.

Claims 28 and 29 are directed, *inter alia*, to methods of treating an individual afflicted with the recited conditions by administering to the individual a therapeutically effective amount of the compound of claims 1 and 3, respectively, or a pharmaceutical composition thereof. The methods of claims 28 and 29 include administering a compound within the genus of proposed count 1 and therefore correspond thereto.

'496 Application

The '496 Application's claim 64 corresponds identically to proposed count 1.

Claim 67 is directed to pharmaceutical composition including a compound defined by claim 64 and proposed count 1.

Proposed count 2.

Proposed count 2 defines a genus of compounds structurally and patentably distinct from the compounds of proposed count 1. The genus of compounds defined by proposed count 2 includes compounds having the generic structural formula of proposed count 2, which includes compounds having a non-bulky substituent at the bridging carbon while having a substituent at position R5 (that is R5 is not H). Proposed count 2 excludes certain Markush groups present, *inter alia*, in claim 1 of the '861 Patent, and claim 1 of the '725 Patent, such that proposed count 2 defines a genus of compounds narrower than the class of compounds defined by those claims.³ This is in part necessary to avoid the prior art.⁴

'861 Patent

Claim 1 of the '861 Patent corresponds to proposed count 2, since claim 1 defines a class of compounds that includes compounds within the scope of the genus defined by proposed count 2.

Claim 2 of the '861 Patent is directed to pharmaceutical compositions including the compounds of claim 1, and therefore corresponds to proposed count 2.

Claim 3 of the '861 Patent depends from claim 1 and narrows the class of compounds defined by claim 1 to compounds wherein R1 is ortho to R2, and R1 and R2 are linked together to form a 5- or 6-membered cycloalkylene ring. The claim includes compounds within the scope of proposed count 2.

Claim 4 of the '861 Patent depends from claim 3 and further narrows the class of

³ See n. 1.

compounds wherein R1 is ortho to R2, and R1 and R2 are linked together to form a 6-membered cycloalkylene ring. The claim includes compounds within the scope of proposed count 2.

Claims 6 and 7 depend from claim 4 and define further subclasses that include compounds within the scope of proposed count 2.

Claim 12 is directed to a species within the scope of the genus defined by proposed count 2, since the compound has a non-bulky substituent in the bridging carbon and a substituent at position R5.

Claim 15 of the '861 Patent is directed to a pharmaceutical composition including a compound of claim 4, while claim 23 is directed to pharmaceutical compositions including a compound from a class of compounds broader than the class of compounds defined by claim 1. The pharmaceutical composition defined by claims 15 and 23 include compounds within the scope of proposed count 2.

'725 Patent

Claim 1 of the '725 Patent corresponds to proposed count 2, since the class of compounds defined by claim 1 includes compounds within the genus of compounds defined by proposed count 2.

Claim 2 of the '725 Patent depends from claim 1 and narrows the class of compounds defined by claim 1 to compounds wherein R1 is ortho to R2, and R1 and R2 are linked together to form a 5- or 6-membered cycloalkylene ring. The claim includes

⁴ See n. 2.

compounds within the scope of proposed count 2.

Claim 3 of the '725 Patent depends from claim 2 and further narrows the class of compounds wherein R1 is ortho to R2, and R1 and R2 are linked together to form a 6-membered cycloalkylene ring. The claim includes compounds within the scope of proposed count 2.

Claims 5, 10 and 13 depend from claim 3. Claim 5 further narrows the class of compounds of claim 3 to those that have an R4 consisting of one of two aromatic carboxylic acids: a pyridine carboxylic acid or benzoic acid. The compounds defined by proposed count 2 have a benzoic acid at this position. Thus, claim 5 includes compounds within the scope of proposed count 2.

Claims 10 and 13 further narrow the class of compounds of claim 3 to specific R3 substituents. As the classes of compounds defined by these claims include compounds having "non-bulky" substituents at R3 and a substituent at R5 - the defining characteristics of the genus of compounds defined by proposed count 2 - these claims also correspond to proposed count 2.

Claims 7, 11 and 14 depend from claim 5. Claim 7 narrows the class of compounds of claim 5 to those where R4 is benzoic acid. Compounds of proposed count 2 also have a benzoic acid at this position.

Claims 11 and 14 further narrow the class of compounds of claim 5 to specific R3 substituents. As the classes defined by these claims include compounds having "non-bulky" substituents at R3 and a substituent at R5, these claims also correspond to proposed

count 2.

Claims 26 and 27 are directed, *inter alia*, to pharmaceutical compositions including a compound within the class of compounds defined by claims 1 and 3, respectively. The pharmaceutical compositions defined by claims 26 and 27 include compounds within the genus of compounds defined by proposed count 2.

Claims 28 and 29 are directed, *inter alia*, to methods of treating an individual afflicted with the recited conditions by administering to the individual a therapeutically effective amount of the compound of claims 1 and 3, respectively, or a pharmaceutical composition thereof. The methods of claims 28 and 29 include administering a compound within the genus of proposed count 2 and therefore correspond thereto.

'496 Application

The '496 Application's claim 65 corresponds identically to proposed count 2. Claim 68 is directed to pharmaceutical composition including a compound defined by claim 65 and proposed count 2.

Proposed count 3.

Proposed count 3 defines a genus of compounds structurally and patentably distinct from the compounds of proposed counts 1 and 2. The genus of compounds defined by proposed count 3 includes compounds having the generic structural formula of proposed count 3, which includes compounds having a bulky substituent at the bridging carbon and a substituent at position R5 (that is R5 is not H). Proposed count 3 excludes certain Markush groups present, *inter alia*, in claim 1 of the '861 Patent, and claim 1 of the '725

Patent, such that proposed count 3 defines a genus of compounds narrower than the class of compounds defined by those claims.⁵ This is in part necessary to avoid the prior art.⁶

'861 Patent

Claim 1 of the '861 Patent corresponds to proposed count 3, since claim 1 defines a class of compounds that includes compounds within the scope of the genus defined by proposed count 3.

Claim 2 of the '861 Patent is directed to pharmaceutical compositions including the compounds of claim 1, and therefore corresponds to proposed count 3.

Claim 3 of the '861 Patent depends from claim 1 and narrows the class of compounds defined by claim 1 to compounds wherein R1 is ortho to R2, and R1 and R2 are linked together to form a 5- or 6-membered cycloalkylene ring. The claim includes compounds within the scope of proposed count 3, which have a bulky substituent in the bridging carbon and a substituent at position R5.

Claim 4 of the '861 Patent depends from claim 3 and further narrows the class of compounds wherein R1 is ortho to R2, and R1 and R2 are linked together to form a 6-membered cycloalkylene ring. The claim includes compounds within the scope of proposed count 3.

Claims 5, 6, 7 and 8 depend from claim 4 and define further subclasses of compounds that include compounds within the scope of proposed count 3.

Claim 15 defines a pharmaceutical composition including a compound within the

⁵ See n. 1.

scope of claim 4.

Claim 23 of the '861 Patent is directed to pharmaceutical compositions. The compositions of claim 23 include a compound within a class defined in claim 23. This class of compounds is broader than the class of compounds defined by claim 1. The pharmaceutical compositions defined by claim 23 include compounds within the scope of proposed count 3, therefore claim 23 corresponds to proposed count 3.

'725 Patent

Claim 1 of the '725 Patent corresponds to proposed count 3, since the class of compounds defined by claim 1 includes compounds within the genus of compounds defined by proposed count 3.

Claim 2 of the '725 Patent depends from claim 1 and narrows the class of compounds defined by claim 1 to compounds wherein R1 is ortho to R2, and R1 and R2 are linked together to form a 5- or 6-membered cycloalkylene ring. The claim includes compounds within the scope of proposed count 3.

Claim 3 of the '725 Patent depends from claim 2 and further narrows the class of compounds wherein R1 is ortho to R2, and R1 and R2 are linked together to form a 6-membered cycloalkylene ring. The claim includes compounds within the scope of proposed count 3.

Claims 5, 10 and 13 depend from claim 3. Claim 5 further narrows the class of compounds of claim 3 to those that have an R4 consisting of one of two aromatic

⁶ See n. 2.

carboxylic acids: a pyridine carboxylic acid or benzoic acid. The compounds defined by proposed count 3 have a benzoic acid at this position. Thus, claim 5 includes compounds within the scope of proposed count 3.

Claims 10 and 13 further narrow the class of compounds of claim 3 to specific R3 substituents. As the classes defined by these claims include compounds having a "bulky" substituents at R3, these claims correspond to proposed count 3.

Claims 7, 11 and 14 depend from claim 5. Claim 7 narrows the class of compounds of claim 5 to those where R4 is benzoic acid. Compounds of proposed count 3 also have a benzoic acid at this position.

Claims 11 and 14 further narrow the class of compounds of claim 5 to specific R3 substituents. As the classes defined by these claims include compounds having a "bulky" substituents at R3 and a substituent at R5, these claims also correspond to proposed count 3.

Claims 12 and 15 depend from claims 11 and 14, respectively, and further narrow the R3 substituent to a few species. As all these species of R3 are "bulky" - one of the defining characteristic of the compounds of proposed count 3, the other being the presence of a substituent at R5 - these claims also correspond to proposed count 3.

Claims 26 and 27 are directed, *inter alia*, to pharmaceutical compositions including a compound within the class of compounds defined by claims 1 and 3, respectively. The pharmaceutical compositions defined by claims 26 and 27 include compounds within the genus of compounds defined by proposed count 3.

Claims 28 and 29 are directed, *inter alia*, to methods of treating an individual afflicted with the recited conditions by administering to the individual a therapeutically effective amount of the compound of claims 1 and 3, respectively, or a pharmaceutical composition thereof. The methods of claims 28 and 29 include administering a compound within the genus of proposed count 3 and therefore correspond thereto.

'496 Application

The '496 Application's claim 66 corresponds identically to proposed count 3. Claim 69 is directed to pharmaceutical composition including a compound defined by claim 66 and proposed count 3.

Proposed count 4.

Proposed count 4 defines a species within the genus defined by proposed count 2. However, this species is patentably distinct, that is, non-obvious over, the genus defined by proposed count 2, because this species has superior and unexpected properties over the compounds in the genus of proposed count 2. See, e.g., *Hester v. Allgeier*, 215 USPQ 481 (CCPA 1982); MPEP 2309.01 ("a count to a species and a count to a genus might properly both be included in the interference if the species is patentable over the genus, even though the genus might not be patentable, given the species").

The superior and unexpected potency of the compound of count 4 is shown by applicants in tables 2 and 4 of the '496 Application. In these tables the compound of proposed count 4 is identified as 3-methyl-TTNEB. Boehm, et al., *Synthesis and structure-activity relationships of novel retinoid X receptor-selective retinoids*, J Med Chem

37(18):2930-41 (1994) (included herewith as Exhibit D) also shows the much superior and unexpected properties of this compound, which in the article is designated 6b. According to the article, this compound is "[t]he most potent compound of the series." Boehm, et al., J Med Chem at 2930 (last line of abstract). The compound is in fact several times more potent than other compounds in the series.

'861 Patent

Claim 13 of the '861 Patent corresponds identically to proposed count 4.

'725 Patent

No claims in the '725 Patent corresponds to proposed count 4.

'496 Application

The '496 Application's claim 70 corresponds identically to proposed count 4.

The terms of the added claims applied to the application are included herewith in a table format as Exhibit E. Further support is also present in the '496 Application.

The requirements of 35 U.S.C. § 135(b) are met for the newly added claims. The '496 Application was filed October 22, 1993, prior to the issuance of the '861 and '725 Patents. In the '496 Application, at least claims 4, 6, 15 and 16 encompassed the subject matter of the newly proposed claims, thus satisfying the requirement of 35 U.S.C. § 135(b).

Other claims in the '496 Application and earlier benefit applications made claims for the subject matter.

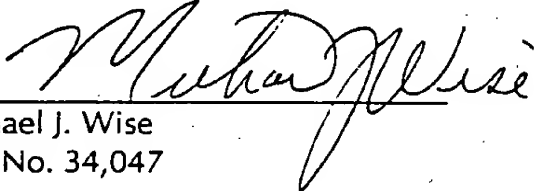
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203/268

The '496 Application has an earlier effective filing date than the '861 and '725

Patents. Accordingly, the requirements of 37 C.F.R. 1.608(a) and (b) are inapplicable here.

Respectfully submitted,

Dated: August 10, 1999

By 
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